Alterations of white matter in different regions in aging and early Alzheimer's disease

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Introduction

With the advent of the diffusion tensor imaging (DTI), there has been a growing interests in investigating the role of the white matter (WM) in neurodegenerative disorders. The neurodegenerative effects of Alzheimer's disease (AD) are well-known and are observed within the somal, dendritic, and axonal compartments. Alterations in DTI values within the WM have been identified with demyelization, degradation of axonal integrity, and a loss of cortical connections. Recent studies have demonstrated that DTI can be used as a method for detecting changes in the WM tracts and the subcortical WM in AD (1,2,3,4). However, these reports are still inconsistent in indicating which WM regions are most affected by AD. Here, we report DTI findings with a large sample size, inclusion of groups of both young and middle-age healthy adults, expansion of the region of interest (ROI), and analyses using three eigenvalues (λ_1, λ_2, and λ_3) together with fractional anisotropy (FA) and trace (Tr) indexes.

Methods

We have performed DTI with 52 subjects: 19 young and middle age controls (YN) (mean age = 38.1, age range 22-60), 18 healthy elder controls (ON) (mean age = 75.6, age 60 and above; mean MMSE = 29 with range 27 - 30) and 15 mildly impaired AD patients (mean age = 75.4, age > 60; mean MMSE = 21 with range 19 - 24). AD patients underwent further neuropsychological evaluations to confirm mild cognitive impairments.

DTI protocol: MRI examinations were performed on a GE Signa 1.5 T MR scanner (LX9.1). In addition to conventional anatomic images, coronal DTI imaging with a single-shot pulsed-gradient spin-echo (PGSE) EPI were performed. Diffusion weightings were applied in 20 different orientations with b value = 0 and 1000 s/mm^2. TR/TE = 8000/85ms, FOV22cm, and matrix128X128. We used 22 contiguous slices perpendicular to the genu-splenium line, approximately 7mm thick, covering WM from the subcortical frontal to posterior parietal and occipital areas. The DTI images were processed using home-built software.

Image analyses: In postprocessed images we computed FA, Tr, λ_1, λ_2, and λ_3 values for 13 regions of interest (ROI)(see Figure 1): **I. Subcortical WM** in the prefrontal region (1) and in the parietal-temporal region (2); **II. Corpus Callosum (CC)**: at the anterior (A), middle (B) and posterior (C) sites; **III. Association fibers**: left and right Cingulum (D) and Superior Longitudinal Fasciculus – SLF (E).

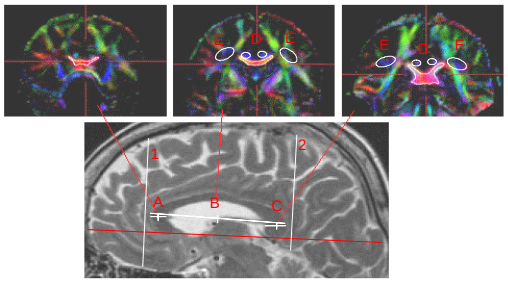

Fig 1. ROIs for subcortical WM (1,2), CC at anterior (A), middle (B), and posterior (C) sites, cingulum (D), and SLF (E).

ROI		FA	Tr	□λ_1	□ λ_2	□ λ_3
CCA	YN	0.58	0.98	1.69	0.83	0.44
	ON	0.52*	1.13*	1.81*	1.02*	0.59*
	AD	0.48	1.18	1.83	1.08	0.62
CCM	YN	0.62	0.85	1.55	0.60	0.40
	ON	0.58*	0.95*	1.67*	0.72*	0.48*
	AD	0.58	1.00*	1.75*	0.75	0.50
CCP	YN	0.53	1.01	1.66	0.81	0.54
	ON	0.52	1.13*	1.86*	0.91*	0.64*
	AD	0.49*	1.19*	1.89	0.99	0.69*

Table 1 Mean FA, Tr, λ_1, λ_2, and λ_3 values for anterior, middle, and posterior CC. * indicates significance between young and old, while * indicates significance between old controls and AD at $p < .05$.

Results

Significant differences between all 3 groups in all ROIs for trace are presented in Fig 2.

Age effects: We observed alterations in WM in almost all ROIs: Tr, λ_1 and λ_2 were significantly increased in all ROIs; the exception was λ_3 value for the right middle cingulum, and right posterior superior longitudinal fasciculus where there was no significance. The rates of Tr increase in WM due to the age-effect were between 10-20 %. FA, however, showed significant decrease in elder controls only for the fibers with the highest anisotropy: anterior and middle CC (Fig 2).

AD effects: In general, AD patients showed changes in diffusivity and anisotropy of WM which were at the same level as changes due to the aging. However, there was a significant decrease in WM anisotropy between AD and elderly participants in the parietal-temporal subcortical WM (Fig 2). There was also a significant decrease in FA for AD patients as compared with old controls in the posterior CC (Fig 2), and a significant increase in diffusivity (Tr) and λ_1 in the middle CC, and an increased Tr and λ_3 in the posterior CC (Table 1, Fig 2). There were no significant changes detected with any measures in anisotropy or diffusivity of WM in the association fibers (Fig 2).

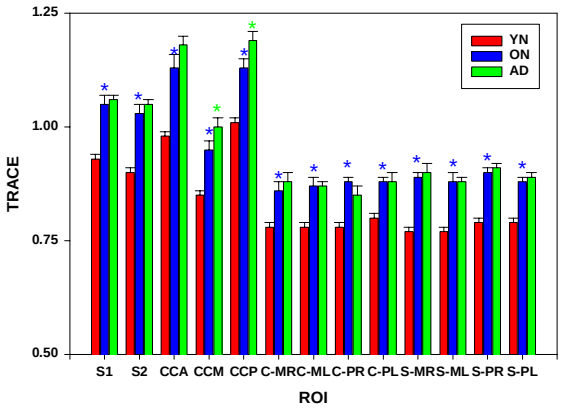

Fig 2 Mean Tr values for all ROIs. * indicates significance between young and old, while * indicates significance between old controls and AD at $p < .05$. Abbreviations: S = subcortical WM, CCA = anterior C, CCM = middle CC, CCP = posterior CC, C = Cingulum, S = SLF; MR = middle right, ML = middle left, PR = posterior right, PL = posterior left

Discussion

Results from this study:

1) showed that the most sensitive measures in detecting age and/or AD effects are λ_1, λ_2, and Tr. FA showed good sensitivity only for the WM tracts (CC) with highest anisotropy.

2) confirmed previous findings regarding the AD effects on the middle and posterior parts of the CC (1, 2). In addition, there were significant decreases in WM integrity at the parietal-temporal regions. The most consistent results with the three indexes (FA, Tr and λ_3) were obtained for the posterior CC (splenium).

3) found very robust age-related effects on diffusivity of WM in almost all ROIs.

Overall, the results showed that age-related effects occurred in all ROIs, with additional WM changes in AD only in the posterior parietal-temporal subcortical WM and in the middle and posterior CC. Age and AD-related changes were more pronounced in tensor trace than FA. These findings, similar to those reported by Head et al. (3), correspond to the initial spread of AD neuropathology from the medial temporal regions to the posterior parietal-temporal sites.

Reference: (1) V. Kavcic et al. ISMRM 2004; 1338. (2) J Zhong, et al. Proceeding of SPIE Medical Imaging. 2004; 5369:238-249. (3) D Head, et al. Cerebral Cortex. 2004;14:410-423. (4) S Takahashi, et al. Neuroscience Letters. 2002;332:45-48.

Acknowledgments: This work was supported by grants from NS43024 and from Schmidt Foundation at University of Rochester.